DEPARTMENT OF HEALTH AND HUMAN SERVICE

Southwest Region

Food and Drug Administration
Denver District Office
Bldg. 20-Denver Federal Center
P.O. Box 25087
6th Avenue & Kipling Street
Denver, Colorado 80225-0087
Telephone: 303-236-3000
FAX: 303-236-3100

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January 25, 2001

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Stephen K. Onody
President and CEO
CMED, Inc.
6175 Longbow Drive
Boulder, Colorado 80301-5388

Ref. #: DEN-01-15

Dear Mr. Onody:

On October 18 through November 21, 2000, Investigator Nicholas R. Nance of our office conducted an inspection of your establishment in Longmont, Colorado. Our investigator determined that your firm manufactures various products under contract, including an electronic controller for a Uterine Balloon Therapy System. These controllers are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System/Good Manufacturing Practice (QS/GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (21 CFR), Part 820. The deviations are as follows:

1. Management reviews of the quality system are not effective in that all quality data is not analyzed, documented and trended, as required by 21 CFR 820.20. For example, your firm does not have adequate trending procedures. Also, there is no evidence that action reports, ECOs, Shipping Hold Forms and related data and in-process inspection defect/quality data are part of your management review.

2. Failure to conduct adequate audits of the quality assurance program to ensure compliance with the established quality system requirements and to determine the effectiveness of the quality system, as required by 21 CFR 820.22. For example, issues identified in prior audits have not been re-audited as required by your firm's procedures, to insure that

corrective actions are complete and adequate. Also, review of your vendor audit schedule revealed that several of your vendor audits scheduled for 2000 have not been completed by the proposed time. Vendors that were found to have problems or defects as a result of your audits still remain on the Approved Vendor List, although there is no indication of corrective action taken.

3. Inadequate corrective and preventative action (CAPA) procedures, as evidenced by:

- Not analyzing all significant sources of quality data, and using appropriate statistical methodology where necessary to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, data from in-process inspection logs, Discrepant Material Tags and e-mail complaints from [redacted] are not included in the Problem Reporting and Corrective Action (PRACA) system. Review of your records also indicates that there is no evidence of evaluation of information regarding nonconformities contained in: Device History Records (DHRs), in-process inspection logs, printed circuit board test records, Rejected Material Reports (RMRs), Discrepant Material Tags (DMTs), Problem Reports, internal and external audit reports, Shipping Holds and complaints. Your CAPA/PRACA system fails to define or identify appropriate statistical methodology to detect recurring quality problems although required by your procedures.

- Not investigating the cause of nonconformities relating to product, processes and the quality systems, as required by 21 CFR 820.100(a)(2). For example, the PRACA system does not always contain all pertinent information regarding nonconformities. Such nonconformities are not always evaluated for root cause. Many RMRs and DHRs indicated significant defects such as overheating and misassembly, however, no corrective actions were noted. Adequate justification is not documented when a decision is made not to investigate or correct a nonconformity.

- Not ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems, as required by 21 CFR 820.100(a)(6). For example, nonconformance reports do not always indicate QA involvement in the MRB evaluation and disposition process as required by your procedures. Discrepancies shown in DMTs, In-process inspection logs and inspection summary data also do not reflect QA review and evaluation.

- Not recording changes in methods and procedures needed to correct and prevent identified quality problems, as required by 21 CFR 820.100(a)(5). For example, your PRACA system does not reflect ECOs, Temporary Deviation Authorities (TDAs) and Shipping Holds issued to correct defects found in your products.

- Although the forms used in your Action Report System database include fields for signature, priority and due date, there is no indication these fields were used. Many of the Action Detail Reports reviewed indicated that they had been open or overdue for several months with no indication that they are being tracked for status.

4. Failure to establish and maintain production process control procedures that describe any process controls necessary to ensure conformance to specifications, as required by 21 CFR 820.70(a). For example, review of DHRs indicated discrepancies in the manufacture of the ThermaChoice II controller, such as the failure to implement required ECOs. There is no evidence that these discrepancies were noted prior to release of devices. Also, inspection methods for final inspection of printed circuit boards are not defined nor is there evidence, when failures do occur, of final disposition or failure investigation.

5. Failure to assure that all elements of design control are addressed when design and process changes are made to a device, as required by 21 CFR 820.30. For example, design modifications have been made to the ThermaChoice II controller as a result of complaints of malfunctions, ineffectiveness or reliability problems. There is no evidence that these design modifications were validated or design controls were addressed. Also, the Design History File was inadequate in that it did not contain any documentation demonstrating design changes made after the initial design transfer in(XXXXX)

6. Statistical techniques are inadequate in that nonconformances are not analyzed to detect recurring quality problems, as required by 21 CFR 820.250. For example,your CAPA/PRACA procedures do not define or identify analytical methods to be used for statistical analysis. Also, your firm has not established action or warning levels to evaluate quality data.

7. Failure to establish and maintain procedures for rework, to include re-testing and reevaluation of nonconforming products after rework to ensure the product meets its current approved specifications, as required by 21 CFR 820.90(b)(2). For example, multiple changes have been made to the ThermaChoice II controller as a result of complaints of poor assembly or poor control of production records. In some cases, complaints were evident indicating that rework performed was ineffective. Also, there is no evidence that all the rework procedures were validated or verified prior to implementation.

8. Failure to establish and maintain procedures for incoming inspection and component acceptance to ensure that all incoming product conforms to specified requirements and that acceptance or rejection is documented, as required by 21 CFR 820.80(b). For example, review of incoming inspection records revealed that component

acceptance/inspection was not always documented. Also, there is no statistical justification for the sampling method used. In some instances, there is evidence that components were accepted without the required sampling.

9. Failure to establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked and maintained, as required by 21 CFR 820.72(a). For example, there are no maintenance records of service/maintenance performed on the ThermaChoice II final test fixture. The [X] catheters used during final test fixture. The [X] catheters used during final testing are not covered by maintenance or repair procedures and controls and were found to have damaged protective shields. Calibration records indicate that periodic calibrations of test equipment have not been performed in a timely fashion, as required by your calibration schedule.

10. Failure to document adequate training of personnel as required by 21 CFR 820.25 (b). For example, review of employee training records revealed that there was no evidence of training for an employee performing incoming inspection of components or of revised ESD procedures for employees working in the printed circuit board area.

11. Failure to review and evaluate all complaints to determine whether an investigation is necessary as required by 21 CFR 820.198(b). For example, numerous instances of device failures were noted in e-mails submitted to your firm from [XXX] These were not handled as complaints and were not entered into your PRACA system.

We acknowledge receipt of your December 11, 2000, response to the FDA form 483 and also acknowledge that you have [XXXXXXXXXXXX] and [XXXXXXXX] [X] We previously issued a post-inspection notification letter to your firm on September 22, 1999, subsequent to our May 12 through June 1, 1999, and our September 7 through 17, 1999, inspections, as a result of corrective actions promised by your firm June 21, 1999. Although the current inspection found that you have made improvements in certain areas, several of the deficiencies found during the 1999 inspections continue to be uncorrected. It has been over a year since the previous inspections, which is sufficient time to have made full correction and to have your quality systems in place.

With regards to your December 11, 2000, response, we have the following comments:

In your response to Management Responsibility, you state that your Management Review Procedure is intended to insure that all relevant topics are addressed your Management Review Process. Although your response stated that the Management Review Procedure was included in the supporting documentation, it must have been inadvertently left out of your response. We are unable to evaluate the adequacy of this response without review of your procedures, however, the various sources of quality data that should be included in Management Review have been outlined above, as well as in the FDA-483 issued at the conclusion of the inspection.

Regarding your response to Corrective and Preventive Action, section B(1)(b), your response states that "Acute issues will be managed expeditiously based upon the nature of the defect and/or failure." Your response does not indicate what you would consider to be acute issues, nor do you define what expeditiously means. It is important that your procedures clearly define all parameters in order to minimize any ambiguity and to successfully implement them. In your response to section B(1)(g), you state that the use of statistical process control is being deleted as it is not appropriate. Our observation was that you were not following your own procedures. If these procedures are not applicable or appropriate, your system must be revised to reflect your operations.

In the area of Design Controls, it is important for you to document the rationale behind the decision of whether a change to a device requires or does not require design reviews. Many of the changes our investigator reviewed did not have evidence of validation or verification. Documentation contained in the ECOs was not adequate to determine if design reviews had been considered prior to implementation.

Finally, with regards to your response concerning Production and Process Controls, we have the following comments: to section D(1)(a) and (b), you state that you have initiated changes to the Device History Records which will address design related issues and provide implementation/execution assurance and that you will review all Device History Records prior to [XXX] for implementation of ECO [XXX] and [XXX] Your response, however, does not address the units that were already released without these upgrades. Do you intend to recall these units and implement the ECOs? In answer to section D(2)(a), (b) and (c), you state that you have changed the Engineering Change Order form to include and indication of who will do the training, however, there is no indication that the training will occur prior to the implementation of the ECO. Our concern with this observation dealt with the fact that you had similar problems with loose components which was addressed by ECO [XXX] initiated in [XX] [XXX] ECO [XXX] implemented in [XXXXXX], involved the rework of units with loose parts, due to continued complaints of loose components. There was no evidence that ECO [XX] [XX] had been validated or verified and therefore, no assurance that the fix would correct the problem. Although the observation deals primarily with lack of validation of the ECO and the continued need to correct the problem, training is also of importance to the execution of the procedures.

We have received your summarized action plan, showing the status of your corrective actions, as well as a copy of the audit performed by [XXXXXXXX] dated [XXXXXXX] Although our inspection concentrated on the ThermaChoice II production, it is important to take a system-wide approach when evaluating your manufacturing operations. At our next inspection of your facility, we expect ALL your systems to be in place and functioning.

The above identified deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your establishment is in compliance with all

requirements of the Federal regulations. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's quality system. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your Quality System.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the QS/GMP deficiencies are reasonably related will be cleared until the violations are corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made, thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, to resume marketing clearance for Class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) have been submitted, and provide Certificates to Foreign Governments for products manufactured at your facility, we are requesting that you submit certification by an outside consultant to this office on the schedule below. Certification by an outside expert consultant should contain assurance that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirements of the device QS/GMP regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report with certification that you have reviewed the report and that your establishment has initiated or completed all corrections called for in the report.

The initial certifications of audit and corrections, and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

- Initial certifications [redacted]
- Subsequent certifications – [redacted]

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by us without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

You should notify this office in writing within fifteen (15) working days of receipt of this letter of any other additional steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to Regina A. Barrell, Compliance Officer, Food and Drug Administration, Denver District, P. O. Box 25087, Denver, CO 80225-0087. If you have any further questions, please feel free to contact Ms. Barrell at (303) 236-3043.

Sincerely,

Thomas A. Allison
District Director